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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/636,530	08/10/2000	Thomas L. Cantor	532212000300	7117

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EXAMINER
JIANG, DONG

ART UNIT	PAPER NUMBER
1646	14

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/636,530	CANTOR, THOMAS L.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's preliminary amendment in paper No. 13, filed on 21 January 2003 is acknowledged and entered. Following the amendment, claims 1-13 are canceled, and the new claims 14-38 are added.

Currently, claims 14-38 are under consideration.

Formal Matters:

A sequence error is found in CRF submitted by the applicants. The error is: the amino acid Asparagine (N) at the position 71 of hPTH (1-84) present in the CRF as SEQ ID NO:1 should be the amino acid Aspartic acid (D) according to published sequence of hPTH, which is represented by Figure 1 in the instant specification. The same error is present in all sequences in the CRF. Appropriate correction is required.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 is indefinite because it is unclear whether "a pharmaceutical PTH antagonist" is intended to mean the protein polypeptide or a pharmaceutical composition thereof. The claim is further indefinite because it is unclear what "conservatively substituted" is intended, and the specification does not define such. The metes and bounds of the claim, therefore, cannot be determined. Claims 18, 22, 26, 30 and 34 are similarly indefinite for the recitation of "conservatively substituted".

Claim 17 is indefinite for the recitation of "further comprising a pharmaceutical carrier". It is unclear how "a ... antagonist" of claim 14 can comprise a carrier.

Claim 18 is further indefinite for the limitation of "*therapeutically* effective". As the preamble merely recites "a method for affecting the binding", it is unclear what "therapeutically effective" is for. Additionally, it is unclear whether the method is for an in vivo use as the terms of "administration" and "therapeutically effective" are used.

Claim 30 is similarly indefinite.

Claim 38 is indefinite because it is unclear what "a pulsatile manner" is meant, and the specification does not define such. The metes and bounds of the claim, therefore, cannot be determined.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-21 and 30-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a method for inhibiting the binding of PTH, or a method for in vivo decreasing calcium ion concentration in blood, does not reasonably provide enablement for claims to a method for *affecting* the binding of PTH (claims 18-21), or a method for in vivo *modulation* of calcium ion concentration in blood (claims 30-33). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 18-21 and 30-33 are directed to a method for affecting the binding of PTH, or a method for in vivo modulation of calcium ion concentration in blood. The claim limitation of "affecting" in claim 18 reads on both stimulating and inhibiting the binding, and the claim limitation of "modulation" in claim 30 reads on both increasing and decreasing calcium ion

concentration. As a PTH antagonist is used in the claimed method, it can only be effective in one way, either stimulating or inhibiting, but not both. As PTH is known to naturally binds to its receptor, and increases blood calcium concentration, a PTH antagonist, such as that of the present invention, would result in *inhibiting* the binding of PTH binding to the receptor, and *decreasing* blood calcium concentration. Additionally, the specification provides no guidance or working examples indicating otherwise (the "stimulating" or "increasing" effect). Therefore, while such methods would be enabled for inhibiting the binding of PTH binding to the receptor, and decreasing blood calcium concentration, they are not enabled for stimulating the binding, or increasing the blood calcium concentration.

Due to the lack of direction/guidance presented in the specification regarding stimulating effect of a PTH antagonist under the claimed conditions, the absence of working examples directed to same, the art indicating the positive effect of PTH on blood calcium concentration, and the breadth of the claims which embrace both stimulating and inhibiting effect of a PTH antagonist, the specification does not enable any person skilled in the art to use the claimed invention in its full scope.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 14-25 and 30-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Fukuda, EP 0 528 271 A1.

Fukuda discloses several hPHT muteins, SEQ ID NOs:19-22, which comprise deletion of 3 to 6 amino acid residues on the N-terminal side of the sequence of hPTH, and teaches that these muteins function as antagonists of hPTH (page 3, lines 12-13). Additionally, Fukuda

indicates that the prior art has established that compounds in which several amino acid residues on the N-terminal side of PTH (1-34) are deleted are known to function as inhibitors (page 3, lines 6-7). Further, Fukuda teaches the application of hPTH antagonists to bone disorders such as hypercalcemia and hyperparathyroidism (page 3, lines 8-9). Although Fukuda does not explicitly teach a *pharmaceutical* antagonist of hPTH, it is well known in the art that a purified protein agent is usually used in combination with other agent(s), such as dissolving solutions, and can not be (rather than) used as its crystal form alone. Dissolving solutions, such as water, buffers, or media, would meet the limitation of "pharmaceutical" or "a pharmaceutically acceptable carrier". As such, Fukuda's hPHT muteins anticipates claims 14-17, and Fukuda's therapeutic application of the hPTH antagonists to hypercalcemia and hyperparathyroidism anticipates claims 18-25 and 30-33.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 26-29 and 34-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fukuda, EP 0 528 271 A1, as applied to claims 14-25 and 30-33 above, and further in view of Kanmera et al., EP 0 451 867.

The teachings of Fukuda are reviewed above. Fukuda does not teach a method for treating renal osteodystrophy or osteoporosis with the hPTH antagonists.

Kanmera discloses peptide derivatives that are PTH antagonists, and teaches that the derivatives exhibit a potent inhibitory activity against hPTH and are useful as a therapeutic agent for treating dysbolism associated with calcium or phosphoric acid, such as osteoporosis and renal osteodystrophy (the abstract).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to apply the PTH antagonists taught by Fukuda in treating disorders such as osteoporosis and renal osteodystrophy as indicated by Kanmera that PTH antagonists are

useful for such disorders. The person of ordinary skill in the art would have been motivated to do so for treating the diseases, and reasonably would have expected success because Kanmera has demonstrated that PTH antagonists are useful as a therapeutic agent.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
3/18/03